PHYS 497B, BIOL 497K
Systems Biology and Networks

Lecturer: Réka Albert

ralbert@phys.psu.edu

122 Davey Laboratory

Network – a tool of understanding complex systems

- Many non-identical elements connected by diverse interactions
- E.g. interaction networks within cells: protein interactions, chemical reactions, gene regulation

- Graph measures provide information on interaction graphs
- Network models explain and predict properties of graph classes

- Network topology influences network robustness and the dynamics of flows
- E.g. dynamics of molecular interaction networks determines the behavior of cells.

- Understand emergent properties – synchronization, differentiation, homeostasis

Suggested reading on networks

1. A.-L. Barabási, Linked: The new science of networks.
2. D. J. Watts, Six degrees: The science of a connected age.

3. G. Caldarelli, Scale-Free Networks: Complex webs in nature and technology.
4. M. Newman, Networks: An Introduction.

5. Buchanan et al, Networks in Cell Biology
6. Bernhard Palsson, Systems Biology: Properties of reconstructed networks
7. Uri Alon, An introduction to Systems Biology

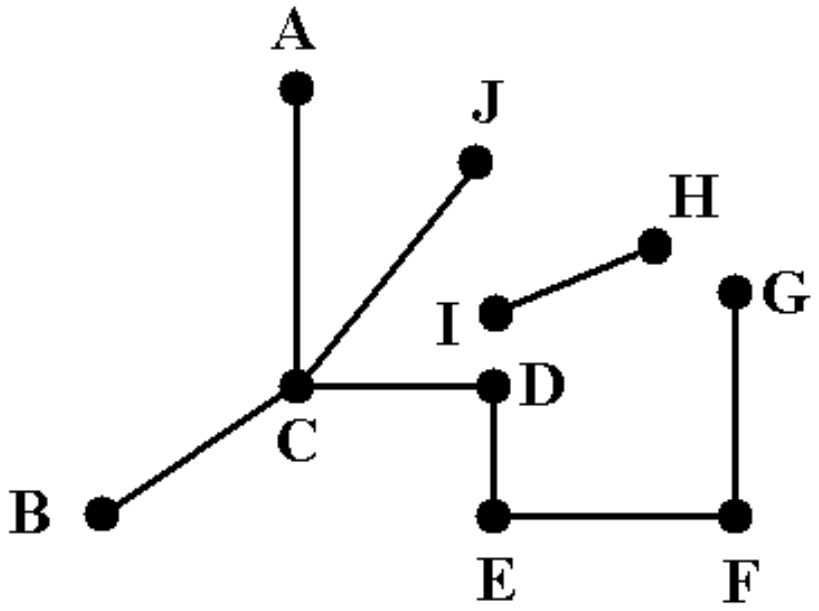
Systems Biology

Multiple working definitions:

- The field that studies how the interactions among the components of a biological system lead to its function and behavior
- An approach that aims to characterize system-wide properties with a unified theoretical explanation
- A cycle composed of predictive modeling of a system, experimental testing of the predictions, and using the newly acquired data for refinement of the model
- Integration and analysis of “-omics” data

A network view is instrumental in all of these definitions.

Definition of graphs (networks)



Network (graph): a set of nodes connected by edges

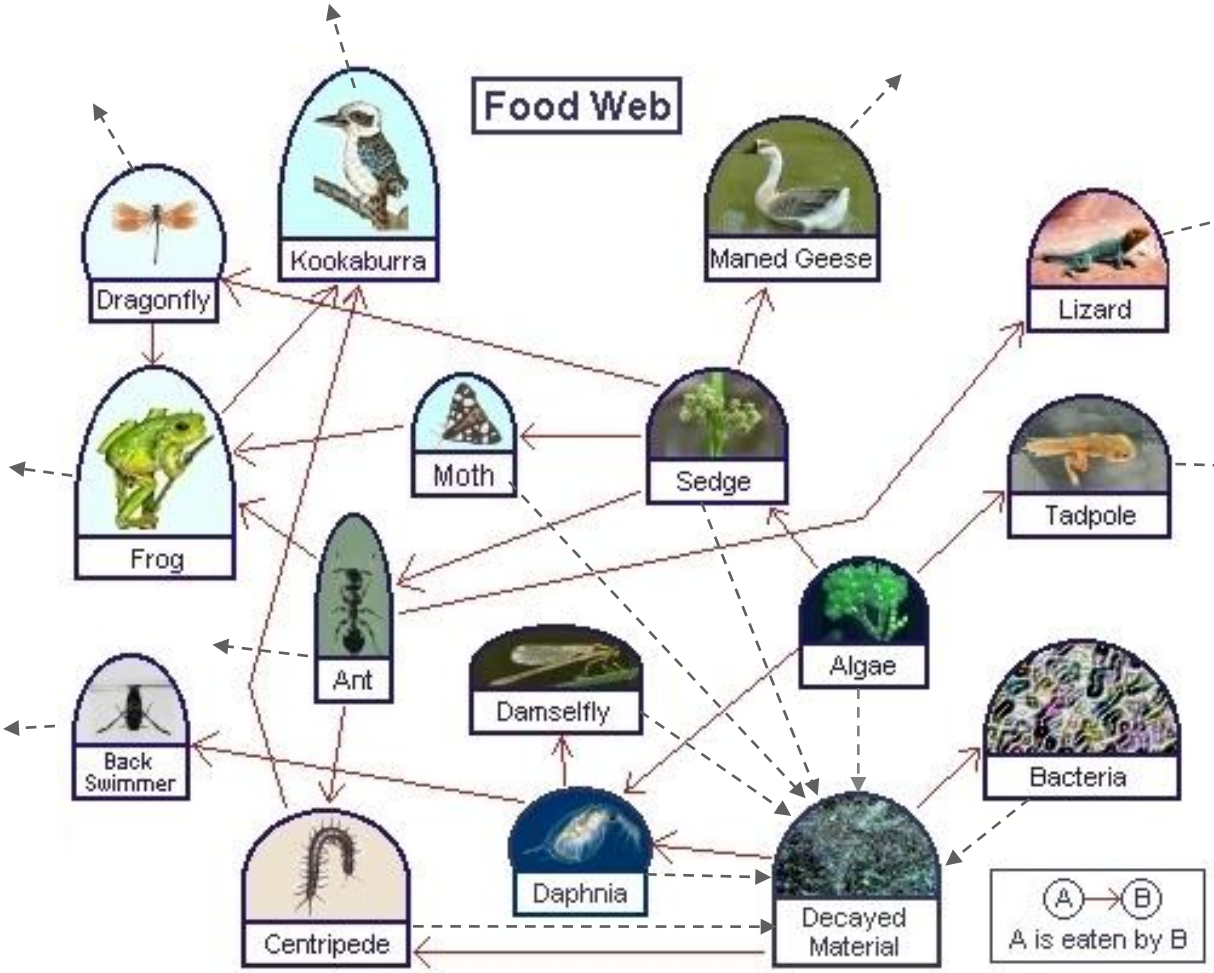
Nodes (vertices): A, B, C…

Edges (links): AC, BC, CD, CJ …

The spatial arrangement of nodes and edges does not matter.

Can be augmented by additional node and edge information.

Food webs describe the energy flow within species



Nodes: species

Edges: nutrient flow

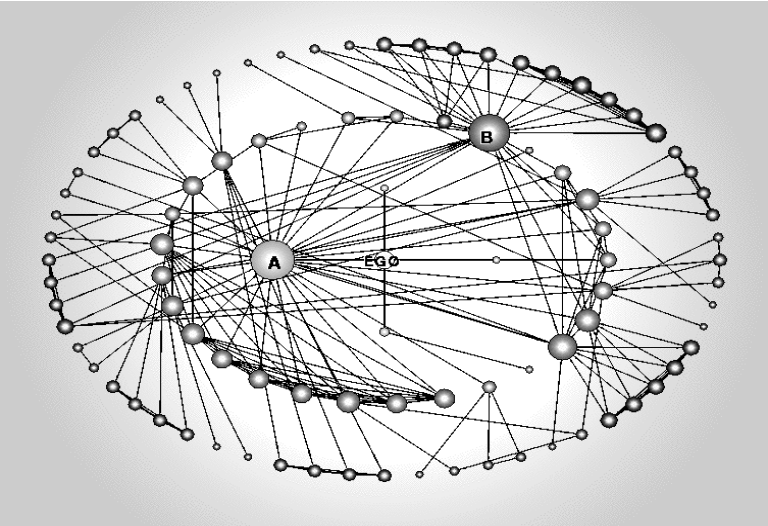
predator-prey relationship →

decay - - - ▸

Directed edges

Q: In what ways is this food web different from a food chain?

Social systems can be regarded as networks



- nodes: individuals
- edges: social interaction
- “six degrees of separation”:

  the social distance between people is small

actor collaboration

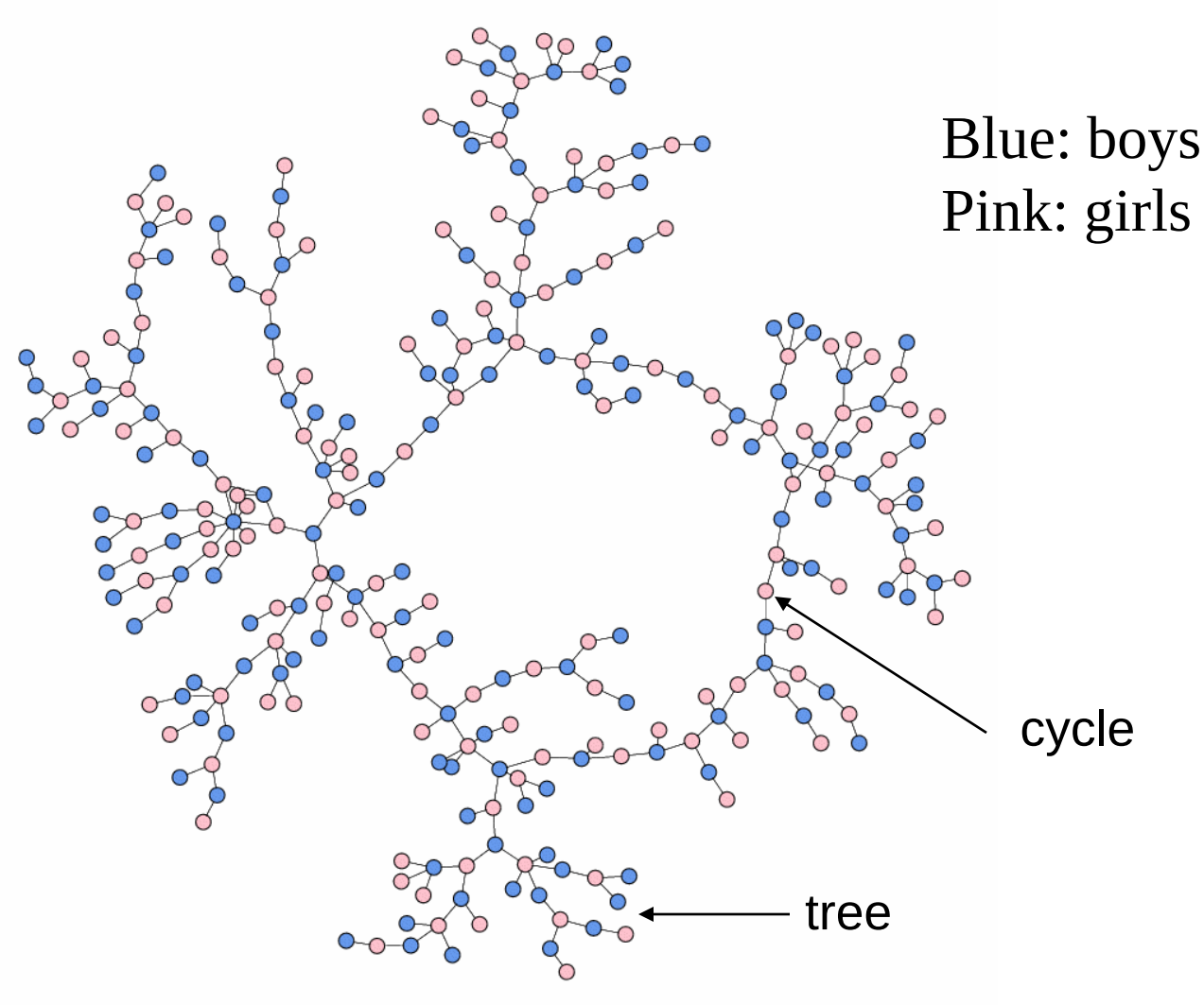
- nodes: actors
- edges: cast jointly

scientific coauthorship

- nodes: scientists
- edges: wrote a paper

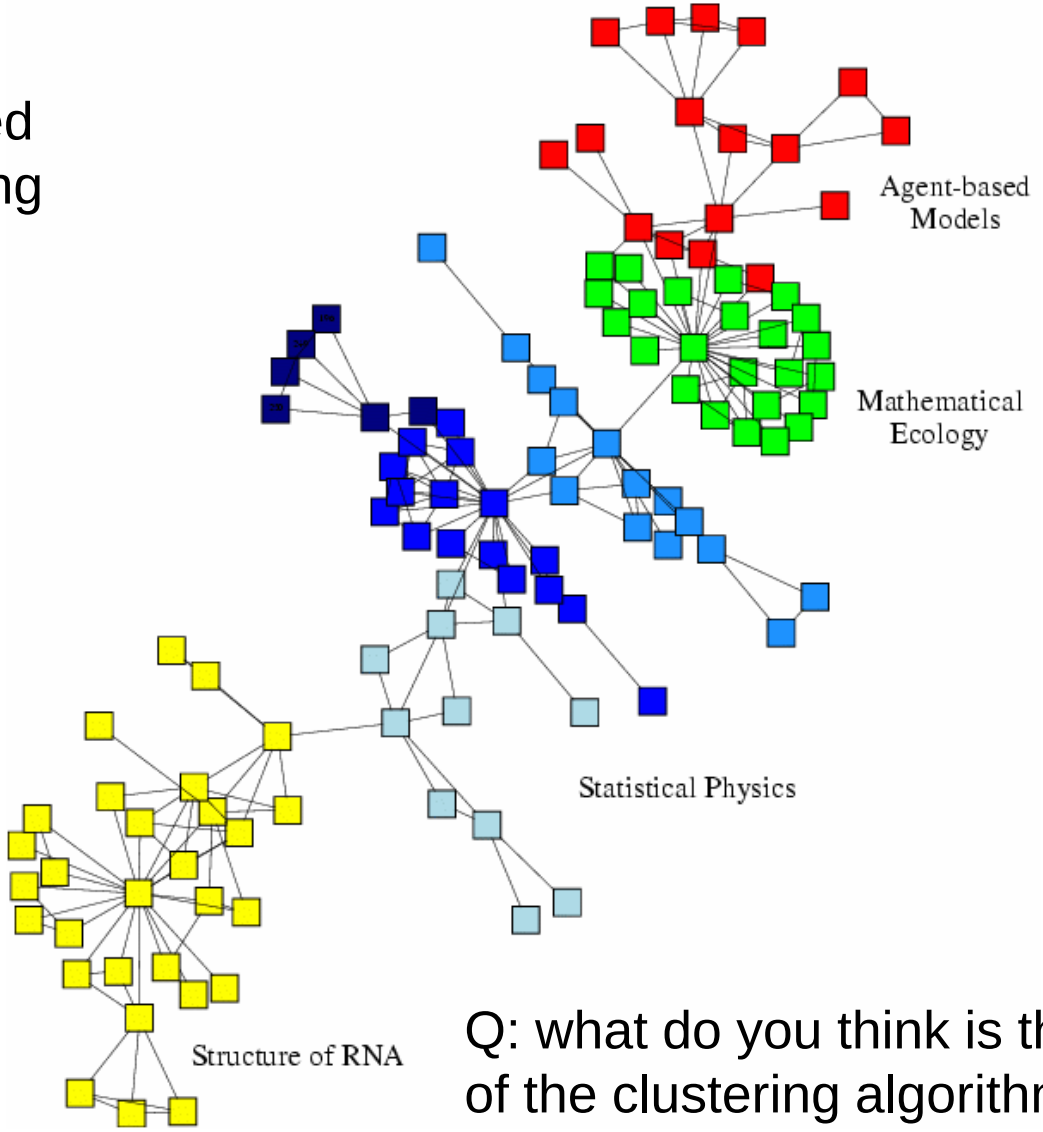
Q: Can you propose an alternative network representation based on actor & movie or author & paper information?

Part of a dating network in a high school



Collaborations at the Santa Fe Institute

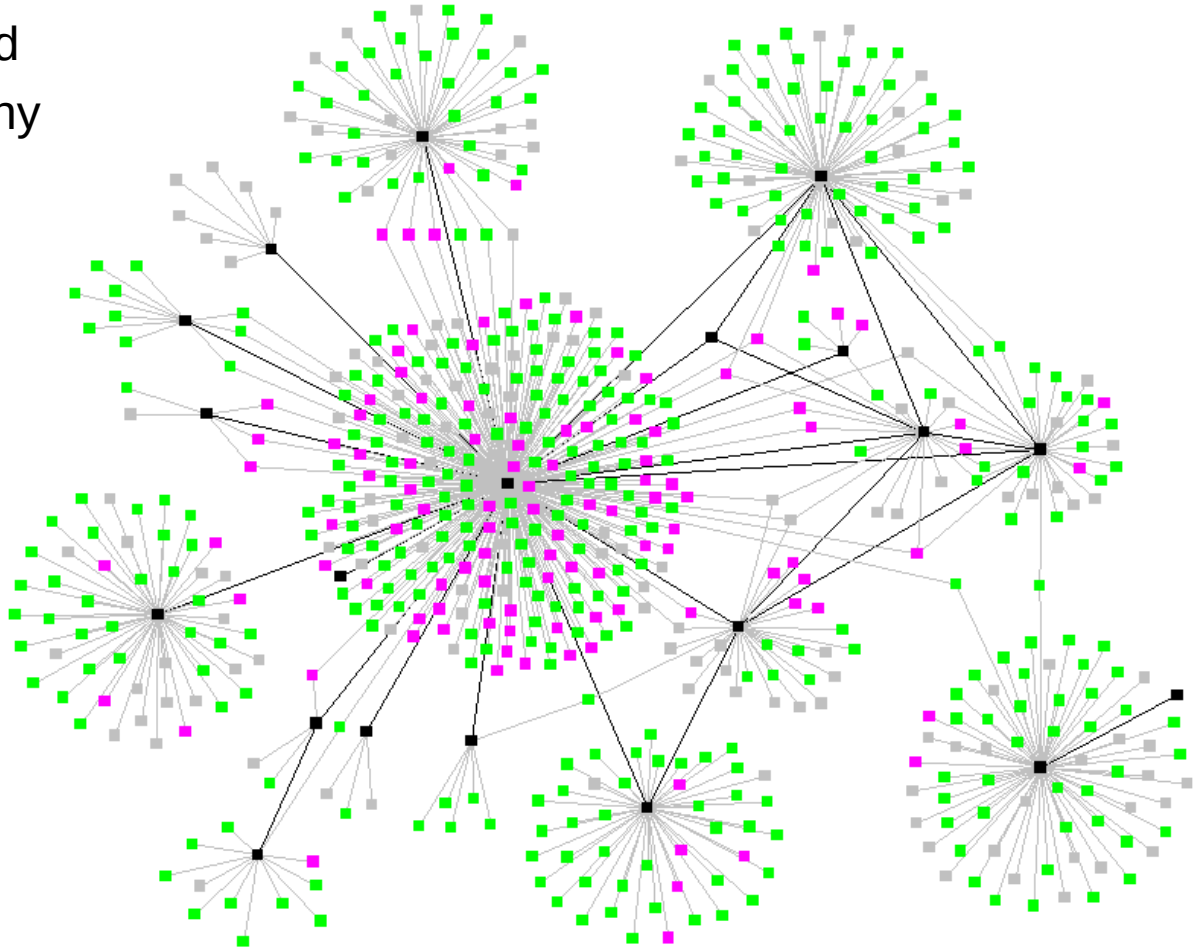
Color: inferred node clustering



Q: what do you think is the basic idea of the clustering algorithm?

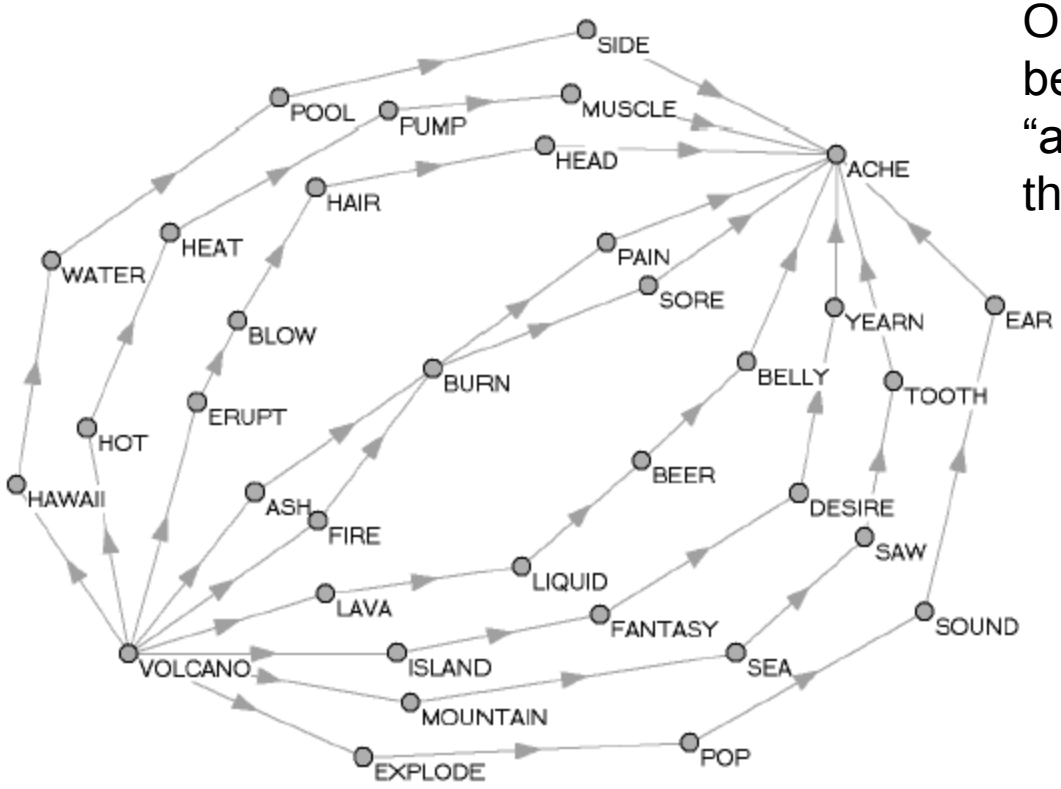
Spread of disease in a social network

- black: diseased
- pink: infected
- green: healthy
- grey: no info



Q: Where do you think the network mapping started?

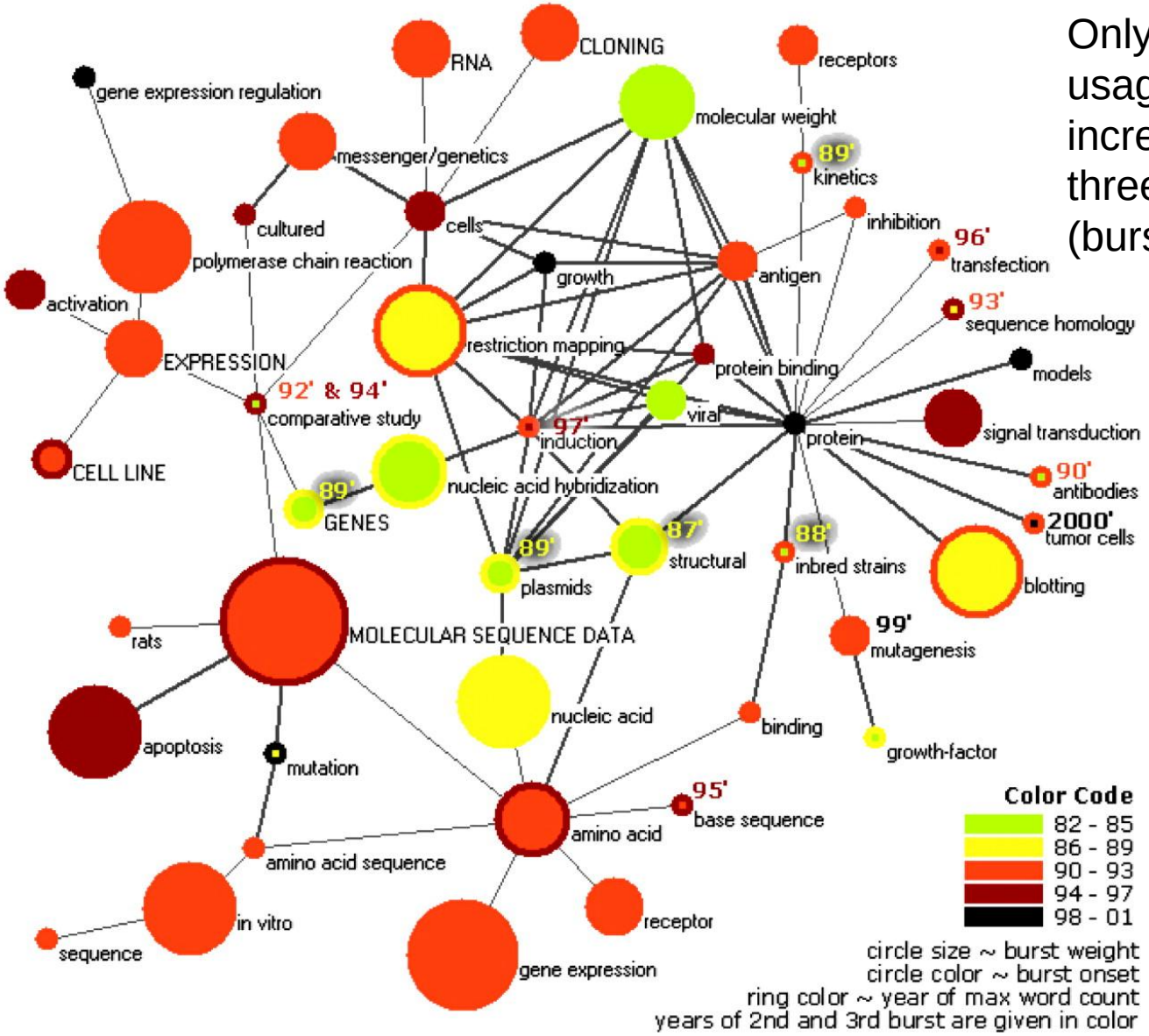
Network of free semantic associations



Only words in paths between “volcano” and “ache” are included in the illustration

Based on the University of South Florida Word Association, Rhyme and Word Fragment Norms

Word co-usage network in PNAS publications



Only words whose usage significantly increased during a three-year period (burst) are included

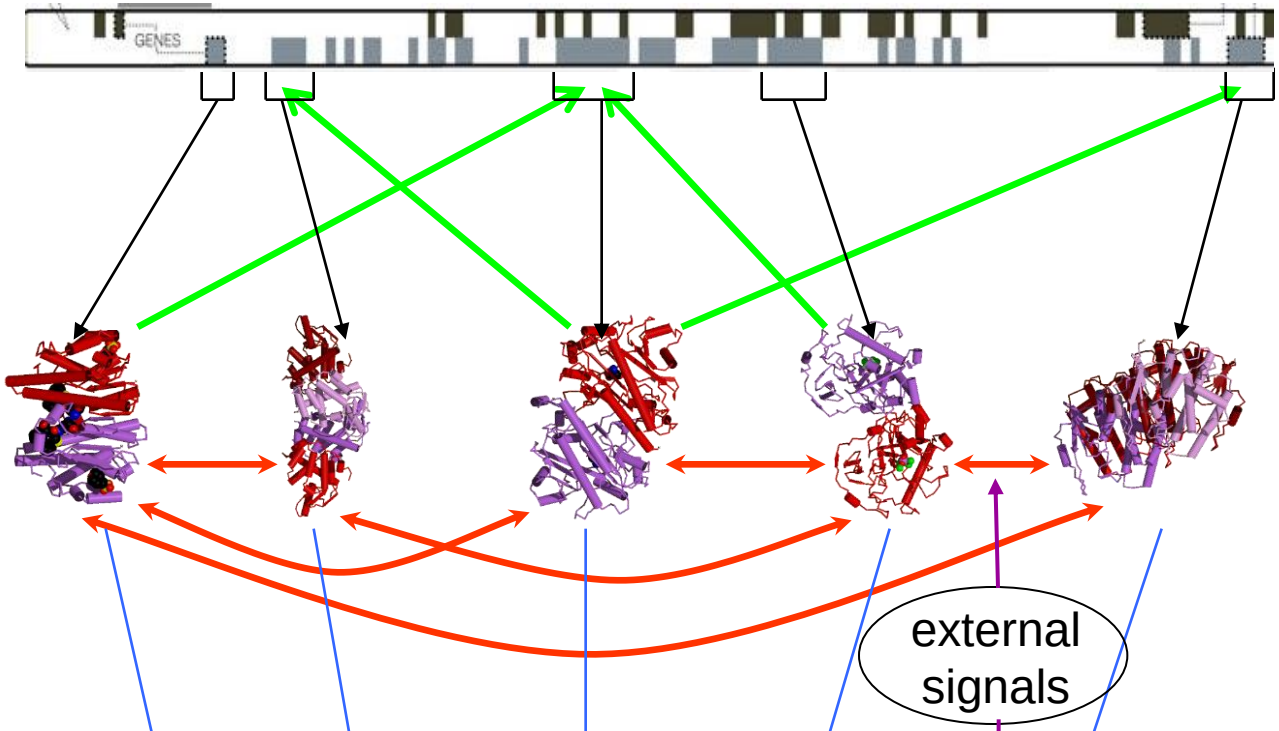
Examples we have seen so far:

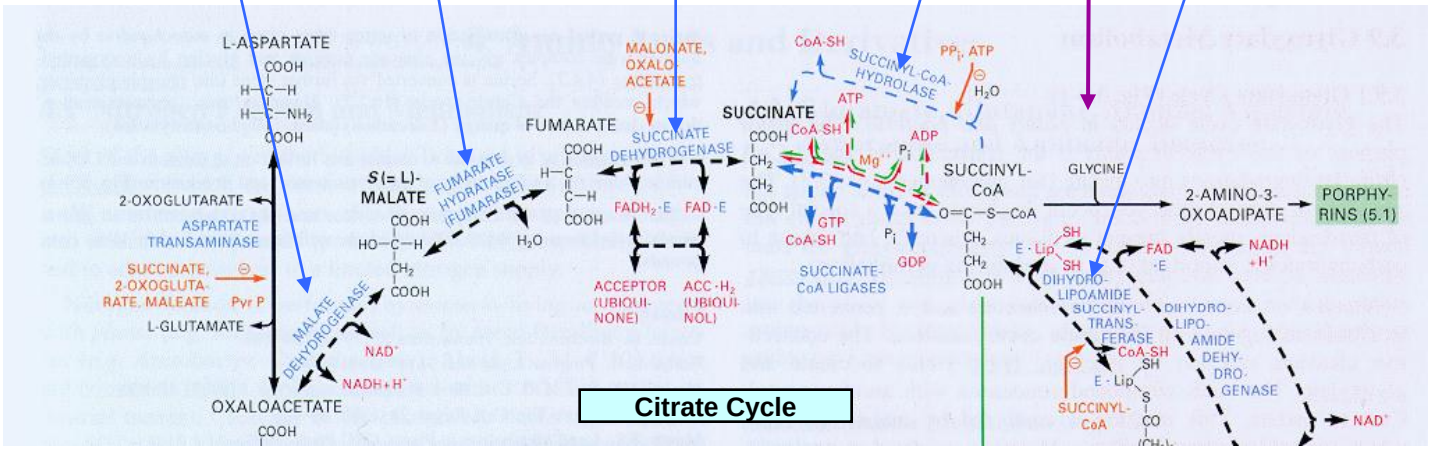
- Food web
- Social networks
- Semantic networks

Focus on the nodes of these networks. In which examples did the nodes represent single entities, and in which did they represent multiple entities or groups?

What additional information do you think is necessary in the latter case?

Many non-identical elements, diverse interactions





GENOME

gene regulation

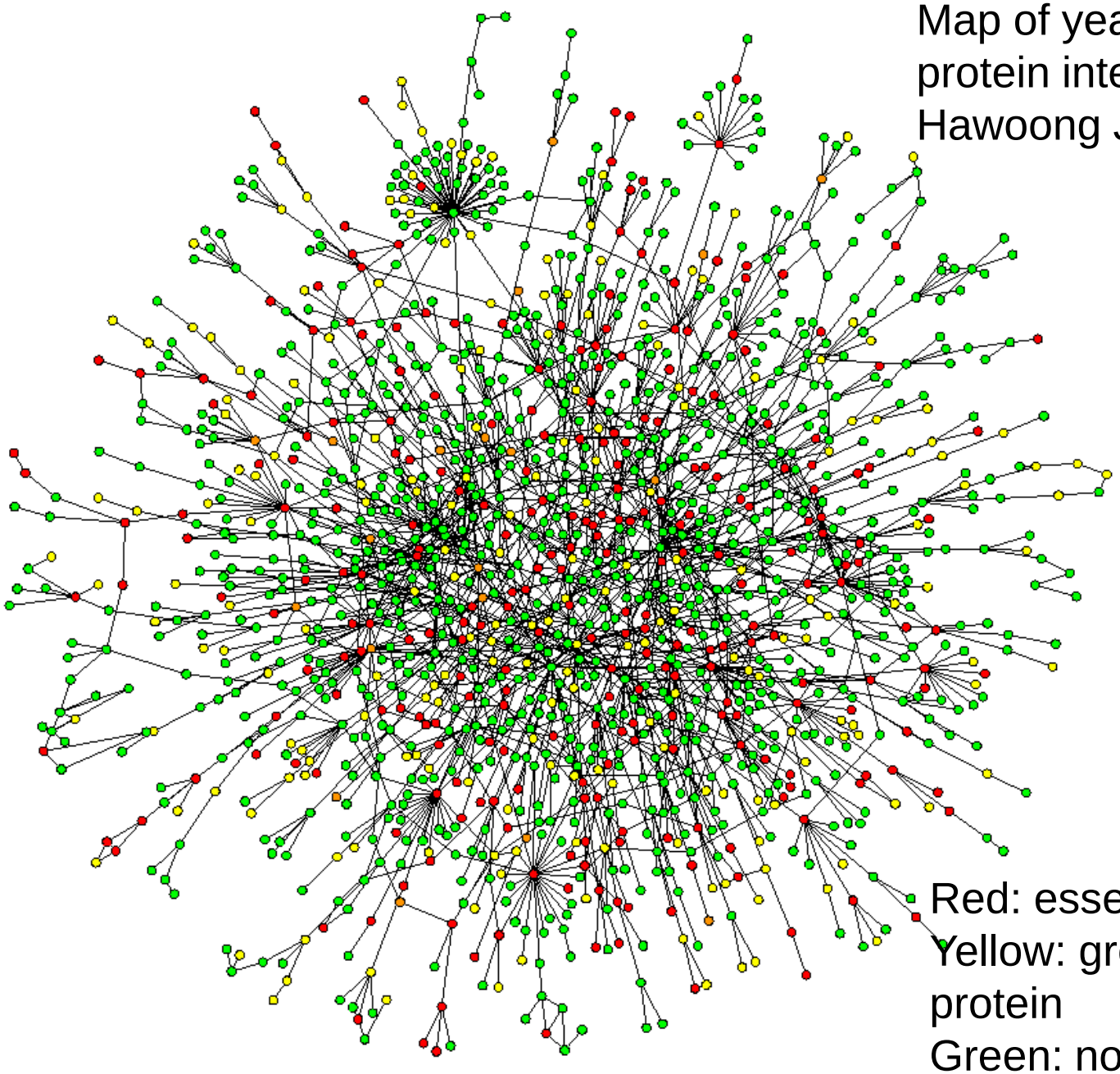
PROTEOME

protein-protein interactions

signal transduction

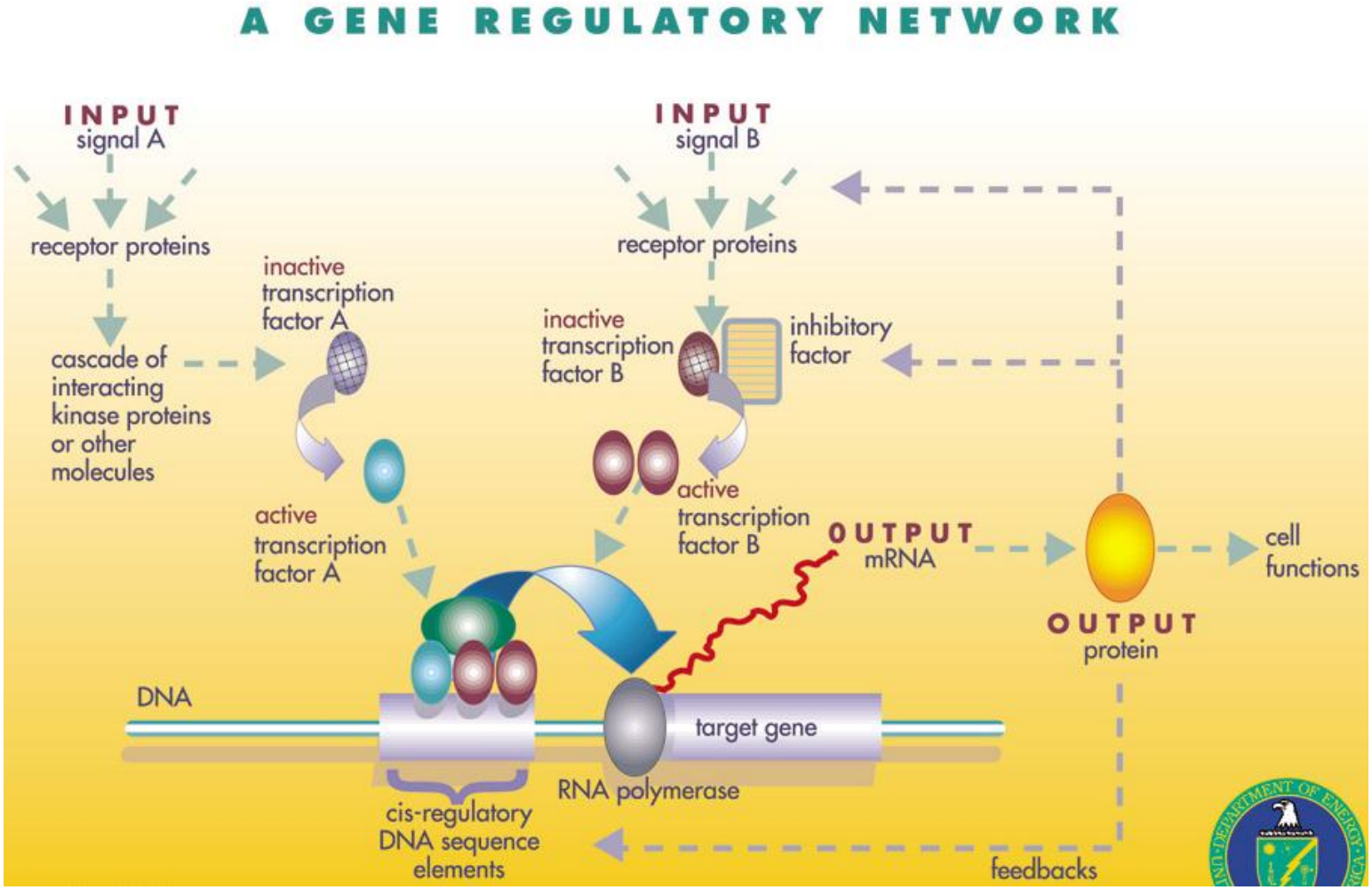
METABOLISM

Bio-chemical reactions



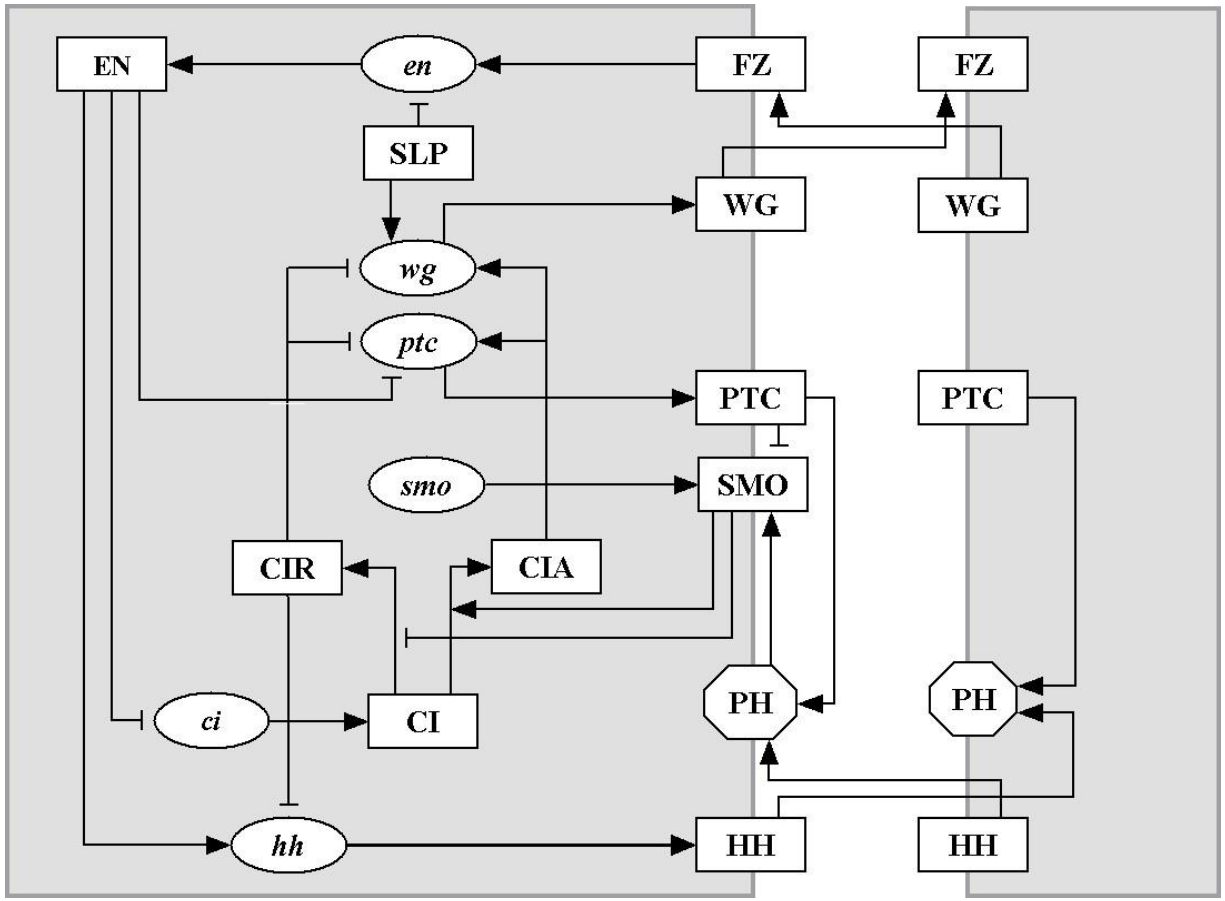
Map of yeast protein-protein interactions, by Hawoong Jeong

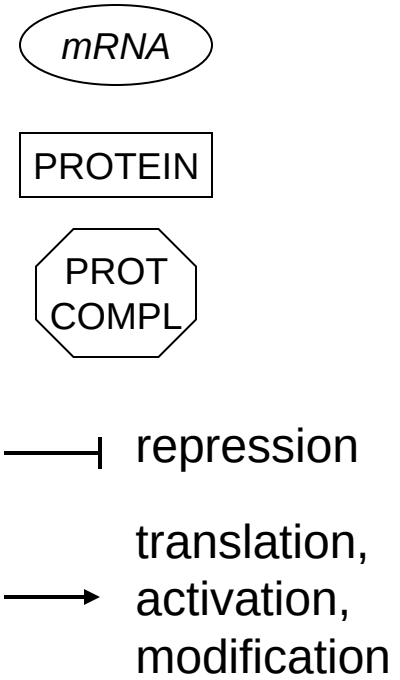
Red: essential protein
Yellow: growth- affecting protein
Green: non-essential protein



Ex: Propose an alternative, less pictorial network representation

Interaction network of the Drosophila segment polarity genes





Albert, Othmer
J. Theor. Bio.
2003

Why study networks and systems biology?

• It is increasingly recognized that complex systems need to be analyzed holistically, and not in a reductionist manner.

• Topological information is fundamental in constructing realistic models for the function of the network.

• Network - related questions:

1. How do we determine or infer network topology ? – E.g. inference of gene regulatory networks

2. How can we quantitatively describe large networks?

3. Why are networks the way they are? – E.g. evolution of protein interaction networks

4. What are the dynamic consequences of a specific network organization?